

General

Guideline Title

Penile cancer.

Bibliographic Source(s)

Alberta Provincial Genitourinary Tumour Team. Penile cancer. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2012 Feb. 9 p. (Clinical practice guideline; no. GU-006). [29 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

For staging definitions, please refer to the Appendix in the original guideline document.

These recommendations have been adapted from the European Association of Urology's *Guidelines on Penile Cancer* (Pizzocaro et al., 2010), the National Cancer Institute's *Penile Cancer Treatment* guidelines (National Cancer Institute, 2009), and the BC Cancer Agency's *Cancer Management Guidelines* on cancer of the penis (Agency BC, 2009).

Institutional Approach

A multi-disciplinary approach encompassing collaboration between the members of the clinical team, especially the surgeon and the radiation oncologist, is recommended for all patients undergoing treatment for penile cancer (Lynch & Pettaway, 2002).

Tis, Ta N0 M0 (Stage 0)

Management Options (National Cancer Institute, 2009)

- Surgical excision with an adequate margin. In order to minimize scarring, deformity, and impaired function, Mohs micrographic surgery is preferred. During Mohs procedure, successive horizontal layers of tissue are excised and examined microscopically.
- Brachytherapy
- Laser therapy in selected cases, using Nd:YAG or CO₂ lasers
- Topical treatment with 5-fluorouracil cream in cases of erythroplasia of Queyrat and Bowen disease.
- Topical treatment with imiquimod 5% cream, an immune response modifier.
- Cryosurgery in patients with erythroplasia of Queyrat and verrucous penile carcinoma

T1 N0 M0 (Stage I)

Management Options (Pizzocaro et al., 2010; National Cancer Institute, 2009; BC Cancer Agency, 2009)

- Circumcision is standard therapy.
- Wide local excision
- Partial penectomy (1 cm proximal to the lesion) for infiltrating tumours of the glans
- Brachytherapy for tumours that infiltrate the glans (T1, T2, and selected, well differentiated T3 tumours) (Lynch & Pettaway, 2002; Roth et al., 2000)
- External beam radiotherapy for larger tumours or those extending onto the shaft

T2 N0 M0 (Stage II) and T3 N0 M0 (Early Stage III)

Management Options (Pizzocaro et al., 2010; National Cancer Institute, 2009)

- Partial penectomy or radical penectomy, depending on the extent and location of the neoplasm
- Radiotherapy (external beam or brachytherapy)
- Patients should be referred for appropriate use of imaging and needle biopsy, assessment, and discussion of lymph node scintigraphy, and potential sentinel node biopsy prior to surgery.
- Prophylactic groin node dissection

T1-3 N1-2 (Stage III)

Management Options (Pizzocaro et al., 2010; National Cancer Institute, 2009; BC Cancer Agency, 2009)

- Partial penectomy or radical penectomy, depending on the extent and location of the neoplasm
- Antibiotic therapy for a short period then reassessment at six weeks
- Bilateral superficial inguinal dissection could be considered, upon direction by biopsy and imaging findings. Clinically evident regional lymph node metastasis without evidence of distant spread is an indication for groin node dissection.
- Patients with positive lymph nodes in the specimen may be considered for radical radiation therapy.
- Surgery to inguinal lymph nodes and radiation therapy may only be considered as an alternative to radical surgery if patient declines.
- Post-operative adjuvant radiation therapy may be considered to decrease the risk of recurrence.
- Patients who are either not candidates for or who refuse surgery may be considered for radical radiation therapy to lymph nodes.

T4 or N3 or M1 (Stage IV)

Management Options (Pizzocaro et al., 2010; National Cancer Institute, 2009)

- Exenterative surgery in select cases
- Palliative radiotherapy and/or chemotherapy

Metastatic Disease and Adjuvant Therapy

Chemotherapy has been largely ineffective in treating patients with large disease burden (Roth et al., 2000; Sheen et al., 2003; Di Lorenzo et al., 2009; Connell & Berger, 1994; Pettaway et al., 2010; Haas et al., 1999; Bermejo et al., 2007; Pagliaro et al., 2010). Options that have been used in clinical trials include: bleomycin, vincristine, and methotrexate +/- radiotherapy and ifosfamide, paclitaxel, and cisplatin, followed by surgery. There is no established role for adjuvant chemotherapy in patients who have completely resected disease.

Follow-Up

Follow-up of patients who have completed treatment for penile carcinoma allows for the detection of a potential recurrence, which may be curable if the recurrence is regional or loco-regional, as well as the assessment of early or late complications from treatment (Pizzocaro et al., 2010). Follow-up also allows for the periodic review and improvement of current treatment policy (BC Cancer Agency, 2009).

Follow-up traditionally consists of inspection and physical evaluation. Diagnostic imaging with ultrasound and PET scan are also useful modalities (Scardino et al., 2004). As approximately 92% of all recurrences occur within the first five years (Crook et al., 2005) after which recurrences tend to be local or new primaries, it is important to provide intensive follow-up for the first two years with less frequent follow-up thereafter (Pizzocaro et al., 2010).

The following schedule of follow-up intervals is recommended (Pizzocaro et al., 2010):

- For patients who have received penile-preserving treatment of primary tumour:
 - Years 1 and 2: every 3 months regular physician or self-examination
 - Years 3, 4, and 5: every 6 months regular physician or self-examination
 - Minimum follow-up: 5 years
 - Follow-up following penile brachytherapy will be more frequent initially and at the discretion of the treating physician
- For patients who have received amputation as treatment of primary tumour:
 - Years 1 and 2: every 6 months regular physician or self-examination
 - Years 3, 4, and 5: every 1 year regular physician or self-examination
 - Minimum follow-up: 5 years
- For patients undergoing a 'wait-and-see' approach with respect to the inguinal lymph nodes:
 - Years 1 and 2: every 3 months regular physician or self-examination; ultrasound with fine-needle aspiration biopsy
 - Years 3, 4, and 5: every 6 months regular physician or self-examination; ultrasound with fine-needle aspiration biopsy
 - Minimum follow-up: 5 years
- For patients who are pN0 with respect to the inguinal lymph nodes:
 - Years 1 and 2: every 6 months regular physician or self-examination; ultrasound with fine-needle aspiration biopsy
 - Years 3, 4, and 5: every 1 year regular physician or self-examination; ultrasound with fine-needle aspiration biopsy
 - Minimum follow-up: 5 years
- For patients who are pN+ with respect to the inguinal lymph nodes:
 - Years 1 and 2: every 3 months regular physician or self-examination; ultrasound with fine-needle aspiration biopsy
 - Years 3, 4, and 5: every 6 months regular physician or self-examination; ultrasound with fine-needle aspiration biopsy
 - Minimum follow-up: 5 years

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Penile cancer

Guideline Category

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Oncology

Radiation Oncology

Surgery

Urology

Intended Users

Physicians

Guideline Objective(s)

To provide recommendations on management and follow-up options for penile cancer

Target Population

Adults over the age of 18 years with penile cancer

Note: Different principles may apply to pediatric patients.

Interventions and Practices Considered

1. Multi-disciplinary approach to management encompassing collaboration between the members of the clinical team, especially the surgeon and the radiation oncologist
2. Surgical excision with an adequate margin (Mohs micrographic surgery)
3. Radiotherapy (brachytherapy, external beam radiotherapy, radical radiotherapy)
4. Laser therapy in selected cases, using Nd:YAG or CO₂ lasers
5. Topical treatment with 5-fluorouracil cream
6. Topical treatment with imiquimod 5% cream
7. Cryosurgery
8. Circumcision
9. Partial or radical penectomy
10. Referral for appropriate use of imaging and needle biopsy, assessment, and discussion of lymph node scintigraphy, and potential sentinel node biopsy prior to surgery
11. Prophylactic groin node dissection
12. Antibiotic therapy
13. Bilateral superficial inguinal dissection
14. Post-operative adjuvant radiation therapy
15. Exenterative surgery
16. Palliative radiotherapy or chemotherapy
17. Adjuvant chemotherapy for metastatic disease
18. Follow-up (physician or self-examination, ultrasound with fine-needle aspiration biopsy)

Major Outcomes Considered

- Penile preservation rate
- Regional failure rates
- Median survival time
- Overall survival rate

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Question

What are the appropriate management and follow up strategies for penile cancer?

Search Strategy

Entries to Medline, EMBASE, and Cochrane (January 2000 to December 2011) and clinical practice guideline databases were searched for evidence relevant to this topic. Search terms included: penile cancer OR cancer of the penis OR carcinoma of the penis OR penile carcinoma, limited to studies published in English.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Genitourinary Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the [Guideline Utilization Resource Unit Handbook](#) (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (<http://www.agreetrust.org>) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulate the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the [Guideline Utilization Resource Unit Handbook](#) (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was reviewed and endorsed by the Alberta Provincial Genitourinary Tumour Team.

When the draft guideline document is completed, revised, and reviewed by the Knowledge Management Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. The working group members then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it is officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Agency BC. Cancer management guidelines: genitourinary: penis. [internet]. BC Cancer Agency; [accessed 2009 Sep 01].

Bermejo C, Busby JE, Spiess PE, Heller L, Pagliaro LC, Pettaway CA. Neoadjuvant chemotherapy followed by aggressive surgical consolidation for metastatic penile squamous cell carcinoma. J Urol. 2007 Apr;177(4):1335-8. [PubMed](#)

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Crook JM, Jezioranski J, Grimard L, Esche B, Pond G. Penile brachytherapy: results for 49 patients. *Int J Radiat Oncol Biol Phys*. 2005 Jun 1;62(2):460-7. [PubMed](#)

Di Lorenzo G, Carteni G, Autorino R, Gonnella A, Perdona S, Ferro M, Longo N, Rescigno P, Doria F, Faiella A, Altieri V, Palmieri G, Imbinbo C, Mirone V, De Placido S. Activity and toxicity of paclitaxel in pretreated metastatic penile cancer patients. *Anticancer Drugs*. 2009 Apr;20(4):277-80. [PubMed](#)

Haas GP, Blumenstein BA, Gagliano RG, Russell CA, Rivkin SE, Culkin DJ, Wolf M, Crawford ED. Cisplatin, methotrexate and bleomycin for the treatment of carcinoma of the penis: a Southwest Oncology Group study. *J Urol*. 1999 Jun;161(6):1823-5. [PubMed](#)

Lynch DF, Pettaway CA. Tumors of the penis. In: Walsh P, Retik A, Vaughan E, Wein A, editor(s). *Campbell's urology*. Philadelphia (PA): Saunders; 2002. p. 2945-82.

National Cancer Institute. Penile cancer treatment, PDQ summary. 2009.

Pagliaro LC, Williams DL, Daliani D, Williams MB, Osai W, Kincaid M, Wen S, Thall PF, Pettaway CA. Neoadjuvant paclitaxel, ifosfamide, and cisplatin chemotherapy for metastatic penile cancer: a phase II study. *J Clin Oncol*. 2010 Aug 20;28(24):3851-7. [PubMed](#)

Pettaway CA, Pagliaro L, Theodore C, Haas G. Treatment of visceral, unresectable, or bulky/unresectable regional metastases of penile cancer. *Urology*. 2010 Aug;76(2 Suppl 1):S58-65. [39 references] [PubMed](#)

Pizzocaro G, Algaba F, Horenblas S, Solsona E, Tana S, Van Der Poel H, Watkin NA, European Association of Urology (EAU) Guidelines Group on Penile Cancer. EAU penile cancer guidelines 2009. *Eur Urol*. 2010 Jun;57(6):1002-12. [PubMed](#)

Roth AD, Berney CR, Rohner S, Allal AS, Morel P, Marti MC, Aapro MS, Alberto P. Intra-arterial chemotherapy in locally advanced or recurrent carcinomas of the penis and anal canal: an active treatment modality with curative potential. *Br J Cancer*. 2000 Dec;83(12):1637-42. [PubMed](#)

Scardino E, Villa G, Bonomo G, Matei DV, Verweij F, Rocco B, Varela R, de Cobelli O. Magnetic resonance imaging combined with artificial erection for local staging of penile cancer. *Urology*. 2004 Jun;63(6):1158-62. [PubMed](#)

Sheen MC, Sheu HM, Huang CH, Wang YW, Chai CY, Wu CF. Penile verrucous carcinoma successfully treated by intra-aortic infusion with methotrexate. *Urology*. 2003 Jun;61(6):1216-20. [PubMed](#)

Type of Evidence Supporting the Recommendations

The recommendations were adapted from existing guidance (see the "Adaptation" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management and follow-up of penile cancer

Potential Harms

- Early and late complications of treatment
- The risks associated with radiotherapy include soft tissue necrosis and urethral stenosis, at rates of 10% to 20% and 20% to 35%,

respectively.

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Genitourinary Tumour Team synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of Alberta Health Services, Cancer Care

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Alberta Provincial Genitourinary Tumour Team. Penile cancer. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2012 Feb. 9 p. (Clinical practice guideline; no. GU-006). [29 references]

Adaptation

The recommendations were adapted from the following guidelines:

- Pizzocaro G, Algaba F, Horenblas S, Solsona E, Tana S, Van Der Poel H, et al. Guidelines on Penile Cancer 2009. Euro Association Urol 2010.
- National Cancer Institute. Penile Cancer Treatment, PDQ Summary. 2009.

- BC Cancer Agency. Cancer Management Guidelines: Genitourinary: Penis. 2009.

Date Released

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Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

Alberta Health Services, Cancer Care

Guideline Committee

Alberta Provincial Genitourinary Tumour Team

Composition of Group That Authored the Guideline

Not stated

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Genitourinary Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. Alberta Health Services, Cancer Care recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Genitourinary Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [Alberta Health Services Web site](#) .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Dec. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the [Alberta Health Services Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on December 13, 2012. The information was verified by the guideline developer on February 1, 2013.

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